

Risk of breast cancer in female flight attendants: a population-based study (Iceland)

Vilhjálmur Rafnsson^{1,*}, Hrafn Tulinius^{1,2}, Jón Gunnlaugur Jónasson³ & Jón Hrafnkelsson⁴

¹Department of Preventive Medicine, University of Iceland, Soltun 1, 105 Reykjavik, Iceland; Ph: +354 525 5213; Fax: +354 562 2013; E-mail: vilraf@hi.is; ²Icelandic Cancer Registry, Skogarhlid 8, 105 Reykjavik, Iceland;

³Department of Pathology, ⁴Department of Oncology, Landspítali-University Hospital, Reykjavik, Iceland (*Author for correspondence)

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Abstract

Objectives: To study whether increased cancer risk, particularly of cancer types previously related to radiation, was found among cabin attendants, using employment time as a surrogate of exposure to cosmic radiation.

Methods: A cohort of 1690 cabin attendants, 158 men and 1532 women from the Icelandic Cabin Crew Association and two airline companies in Iceland, was established. Cancer sites were ascertained between 1955 and 1997 by follow-up in a cancer registry. The personal identification number of each subject was used in record linkage to population-based registers containing vital and emigration status, reproductive factors and histologically verified cancer diagnosis. Standardized incidence rates (SIR) of different cancer sites in relation to employment time and year of hiring were calculated, as well as predictive values of breast cancer risk for evaluating possible confounding due to reproductive factors.

Results: The total number of person-years was 27,148. Among the women, 64 cancers were observed whereas 51.63 were expected (SIR 1.2, 95% CI 1.0–1.6), and significantly increased risk for malignant melanoma (SIR 3.0, 95% CI 1.2–6.2) was found. Significantly increased risks of overall cancers (SIR 1.3, 95% CI 1.0–1.8) and breast cancer (SIR 1.6, 95% CI 1.0–2.4) were observed among the female cabin attendants when 15 years lag time was applied. Those hired in 1971 or later had the heaviest exposure to cosmic radiation at a young age and had significantly increased risk of overall cancer (SIR 2.8, 95% CI 1.4–4.9) and breast cancer (SIR 4.1, 95% CI 1.7–8.5). Predictive values calculated on the basis of reproductive factors among the cabin attendants and the population, and risk of breast cancer were 1.0 for parous vs. nulliparous, 1.0 for number of children, and 1.1 for age at birth of first child.

Conclusion: The increased risk of breast cancer and malignant melanoma among cabin attendants seems to be occupationally related. The part played by occupational exposures, i.e. cosmic radiation, disturbance of the circadian rhythm, and electromagnetic fields or combination of these factors in the etiology of breast cancer among the cabin crew, is still a puzzle as confounding due to parity appears to be ruled out. The relationship between the sunbathing habits of the cabin crew and the increased risk of malignant melanoma needs to be clarified. There is also an urgent need to elucidate the importance of these findings for today's aviation.

Introduction

Recent incidence and mortality cohort studies on commercial pilots have shown an excess risk of acute myeloid leukemia and malignant melanoma [1–3]. The exposure of concern in these studies was cosmic radiation received during flight operation at high altitude. The melanomas, however, were not attributed to this exposure, but rather to sunbathing, although the sun-

bathing habits of pilots have so far not been the subject of any research. The possible effect of jetlag and disturbances in the circadian rhythm resulting in decreased secretion of the pineal gland hormone melatonin have been suggested as playing a part in the high rates of melanoma [3].

Pukkala *et al.* [4] found an increased incidence of breast cancer and bone cancer among Finnish female cabin crew. They also demonstrated a non-significantly

increased risk of malignant melanoma and leukemia. In a research letter, Lynge drew attention to the increased risk of breast cancer among Danish female cabin attendants, using information from a census [5]. The Finnish study emphasized the occupational exposure to cosmic radiation [4]; however, Mawson has pointed out the possible role of work-related disturbances in biological rhythms in general, and melatonin production in particular, in the etiology of breast cancer among flight attendants [6]. Besides exposure to cosmic radiation, other occupational or occupationally related exposure of pilots and cabin crews has previously been discussed [7], including engine exhaust gases, ozone, electromagnetic fields, radiofrequency radiation and different lifestyle factors.

The aim was to study whether increased cancer risk, particularly of cancer types previously related to radiation, was found among cabin attendants, using employment time as a surrogate of exposure to cosmic radiation.

Methods

Information on Icelandic cabin attendants came from three main sources. These were a computerized members list from the Icelandic Cabin Crew Association and different files obtained from two airline companies—Icelandair and Air Atlanta. Employment time was calculated for each individual as the time interval from the first year of employment as cabin attendants, when they were enrolled into the study, until the last year of such employment, both years included. Each person's identification number, which includes the date of birth, was obtained from the National Registry using the name, date of birth, and home address.

The personal identification number of each subject was used in record linkage to the National Registry in order to confirm date of death or date of emigration. In that way, it was possible to ascertain the vital status of the total cohort. A second record linkage was made to the Icelandic Cancer Registry, which is a nationwide registry of cancer cases, with over 95% histological verification [8]. The third record linkages were made to the register of the Genetical Committee of the University of Iceland to obtain information on reproductive factors.

Person-years were calculated for each person, commencing on the first year of employment or 1955, the first year of the Cancer Registry, whichever came later, and ending with the date of death or emigration, or at the end of 1997, the last year in the follow-up period,

whichever came first [9]. The number of expected cancers was calculated on the basis of person-years for each 5-year age category and the cancer incidence rates for the female and male population in Iceland obtained from the Icelandic Cancer Registry. The ratio between observed and expected number of cancers or the standardized incidence ratio (SIR) was calculated with the 95% confidence interval (95% CI) assuming a Poisson distribution and making use of Byar's approximation [9].

Separate analyses were done allowing a number of years to elapse from the beginning of employment before counting of person-years began, here called lag time. In analyses according to employment time, the counting of person-years started in the year in which the person had held the position for the stipulated numbers of years. From the companies' record, it was not possible to identify part-time work or irregular leave, e.g. maternity leave. Neither was it possible to differentiate between aircraft type or routes the cabin attendants had been flying. The cabin crew had been trained for and worked on all types of aircraft the companies had in operation during their employment time [3]. According to information from the companies, they started to run the first jets gradually. In the year 1967 they got the first Boeing 727, and in the year 1971 they took several Douglas DC-8s into operation. This change in the aircraft fleet resulted in a considerable increase in cosmic radiation exposure of the cabin crew, since the vast majority of time they were flying at high altitudes. Radiation exposure, due to nuclear explosion, after age 40 produces a minimal increase in risk for breast cancer, whereas exposure early in life carries a greater risk [10]. A special analysis was carried out on those female cabin attendants who had started employment in 1971 or later, thus focusing on those exposed to cosmic radiation at a young age. In this analysis, 20 years lag time was required since, according to the literature, there is a long latency period for radiation-induced breast cancer [10].

Information on histological type was obtained from the pathology reports.

The information on reproductive factors among the cabin attendants and the Icelandic female population, obtained from the register of the Genetical Committee of the University of Iceland, provided an opportunity to evaluate the possible confounding due to reproductive factors on the risk of breast cancer in the present study in a similar way as has been recommended when evaluating confounding due to cigarette smoking in occupational studies [11]. The relative risk of breast cancer in a sample of the Icelandic female population according to reproductive factors is known from previous studies [12].

Permission was obtained from the Data Protection Commission to establish a file of the cabin attendants and to link the records with other registers.

Results

Altogether 1690 people (1532 women and 158 men) could be identified and were subsequently followed up in the Cancer Registry. The mean age at the start of employment among the women was 23 years (range 19–55), and the mean age at end of follow-up in the year

1997 was 40 years (range 21–76). The numbers of person-years by gender and employment time are shown in Table 1. The cohort is young. Among the women, there were only 276 person-years aged 60 or higher. Among the men, only 0.75 cancers were expected and two cancers were observed – one prostate cancer and one malignant melanoma.

The mean employment time of the female cabin attendants was eight years (range 1–39). Women in the total cohort had increased overall cancer incidence (observed 64 vs. expected 51.63, SIR 1.2, 95% CI 1.0–1.6). Significantly increased risk was seen for malignant melanoma (7 vs. 2.34, SIR 3.0, 95% CI 1.2–6.2). Risk of borderline significance was found for breast cancer (observed 26, SIR 1.5, 95% CI 1.0–2.1). Non-significant excesses were obtained for cancers of the brain, thyroid, bone, Hodgkin's disease and non-Hodgkin's lymphoma (Table 2). Cancer sites with no or one cancer case are shown for the sake of completeness. The mean age of the cancer cases at the year of diagnosis was 43 years (range 24–67), and the mean age of the breast cancer cases at the year of diagnosis was 44 years (range 29–60).

According to the pathology reports, where they decided lobular vs. ductal, all but one of the breast cancers were of ductal type. Of the thyroid carcinomas one was anaplastic, one follicular, and five were of papillary type. The malignant melanomas were all but one of the superficial spreading type. The bone cancer was a chondrosarcoma, and the leukemia was an acute myeloid leukemia.

Table 1. Numbers of male and female cabin crew and person-years according to different employment time and periods of hiring

Categories	No.	Person-years
Total	1,690	28,262.5
Men	158	1,114.5
Women	1,532	27,148.0
With 15 years lag time	871	10,512.5
Two or more years employment	1,111	19,447.0
Five or more years employment	671	11,000.5
Eight or more years employment	448	6,534.5
Ten or more years employment	385	4,917.5
Twenty or more years employment	186	1,448.5
Hired in 1971 or later	1,054	12,746.0
Hired before 1971	478	14,401.0

Table 2. Observed (Obs) and expected (Exp) number of cancers, standardized incidence ratio (SIR) and 95% confidence intervals (CI) among female cabin crew, follow-up during 1955–1997

Cancer sites ^a (ICD-7)	Obs	Exp	SIR	95% CI	
				Lower	Higher
All cancers (140–205)	64	51.63	1.2	1.0	1.6
Stomach (151)	1	0.85	1.2	0.0	6.6
Lung (162)	0	3.35	0.0	–	1.1
Breast (170)	26	17.89	1.5	1.0	2.1
Cervix uteri (171)	4	4.48	0.9	0.2	2.3
Corpus uteri (172)	3	2.04	1.5	0.3	4.3
Ovary (175)	3	3.69	0.8	0.2	2.4
Bladder (181)	1	0.51	2.0	0.0	10.8
Skin melanoma (190)	7	2.34	3.0	1.2	6.7
Other skin (191)	1	0.58	1.7	0.0	9.7
Brain (193)	3	2.22	1.4	0.3	4.0
Thyroid (194)	6	3.88	1.6	0.6	3.4
Bone (196)	1	0.24	4.3	0.1	23.3
Hodgkin's disease (201)	2	0.53	3.8	0.4	13.6
Non-Hodgkin's lymphoma (200, 202)	2	0.97	2.1	0.2	7.5
Leukemia (204)	1	0.96	1.0	0.0	5.8
All other cancers (141, 150, 176)	3	7.10	0.4	0.1	1.2

^a For sake of completeness sites with no or one cancer case are shown.

When allowing 15 years to elapse since recruitment, a borderline excess risk was found among the women for all cancers (observed 52 vs. expected 38.77, SIR 1.3, 95% CI 1.0–1.8). The risk was significantly increased for breast cancer (24 vs. 15.20, SIR 1.6, 95% CI 1.0–2.4). A non-significantly increased risk was found for several cancer sites: the uterine cervix, malignant melanoma, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, and leukemia.

Table 3 shows the observed and expected number of selected cancer sites and SIR according to different employment time of the cabin attendants. Cancer sites with only one cancer case are shown because the sites have been related to radiation exposure in other studies. The SIR for all cancers, breast cancer and malignant melanomas increased with increasing employment time up to 8 or more years of employment. Significantly increased risks were seen for all cancers, breast cancer and malignant melanomas among those with at least 2 and at least 5 years of employment. Among those with at least 8 years of employment, a significantly increased risk for all cancers and breast cancer was found. There was no significantly increased risk for any cancer among those with at least 10 or 20 years of employment; however, the SIRs for breast cancers were 1.6 in the two last named groups.

Table 4 shows the observed and expected numbers of selected cancer sites and SIR among those hired in 1971 or later with and without the requirement of 20 years lag time. Cancer sites with only one cancer case are shown because the sites have been related to radiation exposure in other studies. Significantly increased risks were seen for all cancers, breast cancer and malignant melanomas, independent of employment time (analysed for at least 1, at least 2, and at least 8 years of employment). The mean age of the cancer cases at the year of diagnosis was

37 years (range 24–46), and the mean age of the breast cancer cases at the year of diagnosis was 40 years (range 29–46). When 20 years lag time was allowed between hiring and counting of person-years, the women with one or more years of employment had significantly increased overall cancer incidence (SIR 2.8, 95% CI 1.4–4.9), and breast cancer incidence (SIR 4.1, 95% CI 1.7–8.5). The women with two or more years of employment, and 20 years lag time, also had significantly increased overall cancer incidence (SIR 2.7, 95% CI 1.2–5.3) and breast cancer incidence (SIR 4.0, 95% CI 1.3–9.3). Those with eight or more years of employment, and 20 years lag time, also had significantly increased overall cancer incidence (SIR 4.3, 95% CI 1.7–8.8) and breast cancer incidence (SIR 5.7, 95% CI 1.5–14.6). The women who had started working before 1971 had overall cancer incidence near unity (SIR 1.1, 95% CI 0.8–1.5) and non-significantly increased incidence for breast cancer (SIR 1.2, 95% CI 0.7–1.9), not tabulated.

Table 5 shows the relative risk for reproductive factors in a sample of the Icelandic female population and prevalence of reproductive factors in the population and the cabin attendants. Using the relative risks from the population sample we obtain the predictive value of $(105.24/104.51) = 1.0$ for parous vs. nulliparous. The predictive value was $(97.47/95.36) = 1.0$ for number of children and $(128.15/114.75) = 1.1$ when taking age at birth of first child into account.

Discussion

The excess of breast cancer and malignant melanoma is the most significant finding in the present study. The excess of breast cancer is particularly high for the

Table 3. Observed (Obs) and expected (Exp) number of selected cancer sites and standardized incidence ratio (SIR) according to employment time, person-years (p-y) in each analysis

Cancer sites* (ICD-7)	Two or more employment years (19,447.0 p-y)		Five or more employment years (11,000.5 p-y)		Eight or more employment years (6,534.5 p-y)		Ten or more employment years (4,917.5 p-y)		20 or more employment years (1,448.5 p-y)	
	Obs/Exp	SIR	Obs/Exp	SIR	Obs/Exp	SIR	Obs/Exp	SIR	Obs/Exp	SIR
All cancers (140–205)	56/38.98	1.4**	38/24.89	1.5**	26/16.62	1.6*	20/13.56	1.5	6/6.15	1.0
Breast (170)	22/13.36	1.7*	15/8.74	1.7*	11/5.99	1.8*	8/5.03	1.6	4/2.54	1.6
Skin melanoma (190)	7/1.66	4.2***	5/1.07	4.7**	2/0.72	2.8	2/0.57	3.5	0/0.22	0
Thyroid (194)	3/2.96	1.0	2/1.76	1.1	1/1.12	0.9	1/0.89	1.1	0/0.33	0
Bone (196)	1/0.17	5.9	1/0.12	8.6	0/0.08	0	0/0.06	0	0/0.02	0
Leukemia (204)	1/0.72	1.4	1/0.43	2.3	1/0.28	3.6	1/0.22	4.6	0/0.09	0

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

* Sites with only one cancer case are shown because the sites have been related to radiation exposure in other studies.

Table 4. Observed (Obs) and expected (Exp) number of selected cancer sites and standardized incidence ratio (SIR) among female cabin attendants hired in 1971 or later according to accumulated years of employment, with and without 20 years lag time, person years (p-y) in each analysis

Cancer sites ^a (ICD-7)	One or more employment years			Two or more employment years			Eight or more employment years		
	20 years lag time (1,207.0 p-y)			20 years lag time (8,730.5 p-y)			20 years lag time (916.5 p-y)		
	Obs/Exp	SIR		Obs/Exp	SIR		Obs/Exp	SIR	
All cancers (140-205)	24/14.88	1.6*		20/10.91	1.8**		9/4.92	1.8*	
Breast (170)	10/4.40	2.3*		8/3.26	2.5*		4/1.67	2.4	
Skin melanoma (190)	4/1.04	3.8*		4/0.73	5.5**		1/0.30	3.3	
Thyroid (194)	4/1.50	2.7		2/1.08	1.95		0/0.22	0	
Hodgkin's disease (201)	1/0.29	3.5		1/0.20	5.1		0/0.0005	0	
Non-Hodgkin's lymphoma (200, 202)	1/0.32	3.2		1/0.24	4.2		0/0.08	0	
Leukemia (204)	1/0.36	2.8		1/0.25	4.1		0/0.05	0	
							1/0.10	10.4	
							0/0.03	0	

** $p < 0.01$; * $p < 0.05$.^a Cancer sites with only one cancer case are shown because the sites have been related to radiation exposure in other studies.

subgroup hired in 1971 or later. This is in agreement with the previous Finnish study on cabin attendants [4] and could be related to cosmic radiation. A cabin crew may be exposed to up to 9 mSv per employment year [13], a dose which is well within the permitted limits for occupational exposure to radiation of an adult. The cosmic radiation differs from the exposure in the nuclear industry because of a larger proportion of neutrons. The results are in agreement with findings from atomic-bomb survivors showing that radiation exposure at a young age carries a higher risk for breast cancer than exposure at older age [10]. In the present study, the latency period seems to be at least 20 years, as has been the experience with the atomic-bomb survivors [10]. The mean age of the breast cancer cases at diagnosis was unusually low: 43 and 40 years as compared with the average age for the diagnosis of breast cancer cases reported to the Cancer Registry, which is 60 years [8].

Malignant melanomas were in excess among the cabin crew and have also been found in excess among pilots [1-3]. However, they were not in significant excess among the Finnish cabin crew [4]. The excess of malignant melanoma was again most marked among those hired in 1971 or later, thus among those with the heaviest exposure to cosmic radiation at young age. The distribution of malignant melanoma on the trunk and limbs was thought to indicate sun-exposure as a risk factor among the Danish pilots rather than cosmic radiation [1]. All but one of the malignant melanomas in the present study were located on the trunk and limbs. We have no information on the sunbathing habits of the cabin attendants in our study and, if the malignant melanomas are related to cosmic radiation, we do not know what distribution to expect. The one case of other skin cancer in this study was a squamous cell cancer; however, basal cell carcinomas are not reported here, as they were not regularly registered in the Cancer Registry during the period of the study. A recent study of the atomic-bomb survivors indicates that malignant melanoma can be induced by radiation [14].

Non-significant excess of cancers of the thyroid, brain, non-Hodgkin's lymphoma and leukemia does fit into the possibility that cosmic radiation contributes to the increased risk of breast cancer. The leukemia was acute myeloid leukemia, the subclass known to be related to radiation. The case of bone cancer was chondrosarcoma which has recently been related to radiation therapy [15], but chondrosarcoma was one of the two cancers of bone in the study of the Finnish cabin attendants [4].

The overall cancer risk in this cohort of cabin crew was increased, and no healthy worker effect was seen. On the other hand, the incidence of all cancers increased with increasing number of years of employment and was

Table 5. Relative risk of breast cancer due to reproductive factors in a sample of the Icelandic female population and prevalence of reproductive factors in the year 1989 among the population and the cabin attendants, born 1930–1964

Reproductive factors	Relative risk in the population sample	Population		Cabin attendants	
		No.	Percentage	No.	Percentage
Parity					
Parous	1.00	49,754	80.4	868	77.2
Nulliparous	1.23	12,139	19.6	257	22.8
Number of children					
1–2	1.00	24,447	49.1	575	66.2
3–4	0.93	20,842	41.9	281	32.4
5 or more	0.81	4,465	9.0	12	1.4
Age at first birth (years)					
<20	1.00	14,245	28.6	24	2.8
20–24	1.15	24,960	50.2	280	32.3
25–29	1.23	8,229	16.5	415	47.8
30–34	1.66	1,825	3.7	121	13.9
>34	1.98	495	1.0	28	3.2

high among those hired in 1971 or later. The cabin attendant in Iceland is not subject to regular or frequent health checks like the pilots, although there was certainly a selection of healthy and otherwise qualified individuals into the group of cabin attendants. The absence of lung cancer in the cohort (3.35 expected) may indicate a healthy lifestyle in general. This deficit does not indicate excessive cigarette smoking in spite of the easy access to tax-free tobacco, nor does it reflect potential risk due to passive smoking [7].

Taking into consideration average block hours flown by cabin attendants in recent years and in the past, the employment time, and measurement of cosmic radiation from other studies [13, 16, 17], we estimate the mean annual radiation dose sustained by the cabin attendants to be 3 mSv. To explain the cancer risk found in the present study these estimates seem low. However, these are conservative estimates as the weighting factor of 10–20 was used for relative biological effectiveness of neutrons, which may be far higher; values of 300–600 have been suggested [18]. A significant increase of dicentric chromosomes in peripheral lymphocytes of Concord pilots compared to controls [19] supports this view. Occupational exposures to the cabin crew other than cosmic radiation of concern for the risk of breast cancer and malignant melanoma are disturbance of the circadian rhythm and the electromagnetic fields [3, 6, 20], which may derange the homeostasis of melatonin. Results from an experimental study indicate that melatonin can inhibit growth of B16 mouse melanoma [21]. It was not possible to separate definitely the role of these risk factors in the present study. However, assuming that the magnitude of exposure to electromagnetic fields was the same before and after 1971 does not indicate

that this exposure alone is important in relation to breast cancer, as the breast cancer risk was confined to those hired in 1971 or later.

It has been suggested that pesticides used in aircraft may contribute to the increased risk of breast cancer among cabin attendants [22] but this is refuted by others [23]. According to information from the Icelandic Cabin Crew Association and Icelandair, pesticides were used in regular flights from Europe to the US while it was necessary to stop in Gander, Newfoundland, during the period 1956–1960. Otherwise pesticide spraying was not carried out, with the exception of sporadic charter flights to subtropical countries. We agree with the view that the strongest factors that have been shown empirically to affect risk of breast cancer among occupational or social groups are parity and age of first child birth [23]. It is clear from the calculations of the predictive values [11] that the risk of breast cancer found to be 1.45 in the total cohort is unlikely to be explained solely by confounding due to parity; nor the excess of breast cancer found among those hired in 1971 or later when the SIR was 2.3, or when applying 20 years latency period the SIR was 4.1. Concern may arise as to whether this evaluation is tempered because of different age distributions in the population and among the cabin attendants. Cohort effects are nevertheless related to the distribution of reproductive factors, which are documented in the present study. According to the National Registry the proportion of women in the population born 1965–1961, 1960–1951, and 1950–1931 was 19.4, 35.4 and 45.2, and the respective proportion in the cohort was 15.8, 34.3 and 49.9.

Because of the limited size of the cohort, we are not able to evaluate the possible relation of cosmic radiation

with the rarer types of cancer such as leukemia, non-Hodgkin's lymphoma, bone cancer and thyroid cancer. The strength of the study is the use of the comprehensive population registries in Iceland, the National Registry, the registry of the Genetical Committee of the University of Iceland, and the Icelandic Cancer Registry. The universal use of the identification numbers made record linkage possible, which ascertained vital and emigration status for all cohort members and secured complete identification of cancer cases in the nationwide Cancer Registry. Approximately 95% of the cancers reported to the Cancer Registry have histologically confirmed diagnoses [8]. The incidence of cancer in the population of Iceland was obtained from the Cancer Registry, thus information on cancer in the cohort and among the population was obtained in the same way.

In conclusion, we have found an increased risk of breast cancer and malignant melanoma among cabin attendants, which seems to be occupationally related. The part played by occupational exposures, i.e. cosmic radiation, disturbance of the circadian rhythm, and electromagnetic fields or combination of these factors in the etiology of breast cancer among the cabin crew, is still a puzzle, as confounding due to reproductive factors appears to be ruled out. The relationship between sunbathing habits of the cabin crew and the increased risk of malignant melanoma needs to be clarified. There is also an urgent need to elucidate the importance of these findings for today's aviation.

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